Claims

1. A process of parallel fractionation of a multiplicity of individual samples (29) in a separation medium (6), which process comprises the following steps:

   a) a first space (2) which essentially extends across all three space coordinates contains the separation medium (6),

   b) a multiplicity of individual samples (29) is arranged close to an interface of the first space (2),

   c) the individual samples (29) are essentially arranged in such a way that the positions of their centers of gravity can be described by two coordinates,

   d) under the influence of one or more physical or chemical parameters, the individual samples (29) migrate through the separation medium (6) and

   e) the sample fractions are detected and, alternatively or additionally, preparatively couected.

2. The process as claimed in claim 1, characterized in that, during migration, the individual samples (29) are detected in selected regions within the separation medium (6) or close to an interface of the separation medium (6).

3. The process as claimed in claim 1 or 2, characterized in that, after completing the migration, the individual samples (29) are detected by a 3D data receiving process, preferably by a 3D image-taking process.

4. The process as claimed in one or more of claims 1 to 3, characterized in that the sample fractions, after passing through the separation medium (6) or after separation has finished, are received, preferably by a fraction couecting device.

5. The process as claimed in one or more of claims 1 to 4, characterized in that, after the separation has finished, the separation medium (6) is cut into disks which may then be evaluated by a 2D detection process and from which, additionally or

alternatively, individual sample fractions may be couected.

6. The process as claimed in one or more of claims 1 to 5, characterized in that electrode elements (4, 5) are arranged in such a way that, when applying an electrical voltage, the individual samples (29) migrate through the separation medium (6) essentially perpendicularly to the plane of their application.

7. The process as claimed in one or more of claims 1 to 6, characterized in that in the first space (2) a temperature distribution is generated and maintained which is essentially independent of a coordinate running perpendicular to the direction of sample migration (14).

8. The process as claimed in one or both of claims 6 and 7, characterized in that the first space (2) perpendicular to the direction of sample migration (14) is thermally insulated.

9. The process as claimed in one or more of claims 6 to 8, characterized in that in the first space (2) and/or in a further space (3), at the particular surface whose normal is perpendicular to the direction of sample migration (14), a temperature profile (60) which essentially corresponds to the temperature profile along the direction of sample migration (14) in the center of the first space (2) is generated and maintained by means of a temperature-control device along the direction of sample migration (14).

10. The process as claimed in one or more of claims 6 to 9, characterized in that the electrically converted Joulean heat in the first space (2) and/or in a further space (3), at the particular end faces whose normal is in the or against the direction of sample migration (14), is removed by means of a temperature-control device.

11. The process as claimed in one or more of claims 6 to 10, characterized in that the first space (2) is enclosed by a further space (3) which contains a solvent, electrolyte or buffer medium (31) which is in contact with the electrode elements (4, 5).

12. The process as claimed in one or more of claims 6 to 11, characterized in that the liquids (31) surrounding the electrode elements (4, 5) are exchanged between said electrode elements (4, 5) by way of circulation.

13. The process as claimed in one or more of claims 6 to 12, characterized in that the dimensions of the separation medium (6) in the first space (2) are such that a ratio of its radial extension (9) to its longitudinal extension (15) of ≥ 0.5, preferably > 1, is obtained.

14. The process as claimed in one or more of the preceding claims, characterized in that the separation medium (6) contained in the first space (2) is polyacrylamide, agarose or hydroxyl cellulose.

15. The process as claimed in one or more of the preceding claims, characterized in that the sample is applied by two-dimensionally arranging the individual samples (29) in or on an essentially two-dimensional sample plate which can be introduced into the separating device (1) from the outside or which is part of the separation medium (6).

16. The process as claimed in claim 15, characterized in that the individual samples (29) are locally fixed in or on the sample plate, preferably via a porous support layer or in or on essentially two-dimensionally arranged point-like depressions or elevations of the sample plate.

17. The process as claimed in claim 15 or 16, characterized in that the individual samples (29) can be localized in or on the sample plate by electrical or magnetic forces.

18. The process as claimed in one or more of claims 15 to 17, characterized in that the individual samples (29) can be transferred between different sample plates, preferably by means of pressure, diffusion, electrical or magnetic forces.

19. The process as claimed in one or more of claims 15 to 18, characterized in that chemical reactions, physical treatments, measurements or separations according to one or more parameters are carried out in or on the sample plates.

20. The process as claimed in one or more of claims 15 to 19, characterized in that the individual samples (29) are preferably present on or in particles, preferably in host organisms, for example yeasts, bacteria or "competent cells".

21. A process of distributing particles in or on a sample plate, characterized in that a

device or a process is used in which the particles are distributed according to measured physical or chemical properties.

22. The process as claimed in claim 21, characterized in that the 2-dimensional distribution of particles, preferably of host organisms, for example yeasts, bacteria or "competent cells", is carried out using a device or process in which said particles are distributed owing to measured properties, preferably in or on a sample plate.

23. The process as claimed in claim 21 or 22, characterized in that the two-dimensional distribution of the particles is carried out using a device or process in which the particles are distributed, for example by a cell sorter or a fluorescence-activated cell sorter (FACS), preferably in or on a sample plate.

24. The process as claimed in one or more of claims 21 to 23, characterized in that in that host organisms, for example yeasts, bacteria, competent cells, are distributed owing to the dyes (e.g. GFP = green fluorescent proteins) produced therein, preferably in or on a sample plate.

25. The process as claimed in one or more of claims 15 to 24, characterized in that the individual samples (29) are multiplied from individual molecules or from a multiplicity of molecules preferably of the same kind, preferably in or on a sample plate.

26. The process as claimed in claim 25, characterized in that the individual samples (29) are multiplied by cloning and subsequent selective propagation, preferably in or on a sample plate into which host organisms such as, for example, yeasts, bacteria or "competent cells" have been distributed by means of the processs as claimed in claims 21-24.

27. The process as claimed in one or more claims 23 to 26, characterized in that the individual samples (29) are multiplied by means of PCR.

28. The process as claimed in one or more of claims 15 to 27, characterized in that the individual samples (29) are arranged in or on a sample plate as fractions of a preseparation or one or more source samples(s).

29. The process as claimed in claim 28, characterized in that the sample plate consists

of or contains a separation medium (6) and the fractions are arranged by separating one or more samples in the sample plate.

30. The process as claimed in claim 29, characterized in that the samples for their part are fractions of one or more preceding separation(s) with preferably different separation properties, which fractions have been transferred to the sample plate by preparative transfer.

31. The process as claimed in one or more of claims 28 to 30, characterized in that the process is used for analyzing protein mixtures or for analyzing metabolic products.

32. The process as claimed in one or more of the preceding claims, characterized in that the sample fractions are detected by means of a confocal detection apparatus (45) such as a spot- or cylindrical-confocal detection apparatus.

33. The process as claimed in claim 32, characterized in that detection is carried out using a confocal detection apparatus (45) containing a confocal multiple measuring head (46).

34. The process as claimed in one or both of claims 32 and 33, characterized in that the sample fractions are detected using a detection apparatus (45) with a multiple measuring head (46) whose optics comprise a gradient index lens field (50), a microlens field, a cylinder lens system or a combination of these elements.

35. The process as claimed in one or more of claims 32 to 34, characterized in that the detection apparatus (45) is movable in the x, y; r, ω direction with respect to a detection area (8) of the first space (2).

36. The process as claimed in one or more of claims 32 to 35, characterized in that the electrode elements (4, 5) are integrated in the detection apparatus (45) and move together with the latter.

37. The process as claimed in one or more of claims 1 to 31, characterized in that the sample fractions are detected using an imaging optics with image recording process, whose optical axis (43) is essentially parallel to the direction of sample migration (14) of the individual samples (29).

38. The process as claimed in one or more of claims 1 to 31, characterized in that the sample fractions are detected using an imaging optics with image-taking process, whose optical axis is essentially tilted with respect to the direction of sample migration (14).

39. The process as claimed in claim 37 or 38, characterized in that the sample fragments are optically excited by widening one or more laser beam(s) (52, 53) through cylinder optics (27, 28) in a fan-shaped manner or by projecting said laser beam(s) laterally or tilted to the direction of sample migration (14) through moving or rotating mirrors into the separation medium (6) in such a way that a planer detection area (8) in said separation medium is illuminated.

40. The process as claimed in one or more of claims 32 to 39, characterized in that the individual samples (29) are labeled with dyes, preferably with fluorescent dyes.

41. A device for carrying out the process as claimed in one or more of the preceding claims, characterized in that

a) the separating structure (1) comprises a preferably cylindrical hollow space (2) which essentially extends across 3 space coordinates,

b) the hollow space (2) is designed so as to be filled with a separation medium (6),

c) a device which enables samples (28) which are to be fractionated at an end face and which are essentially arranged two-dimensionally in a plane to be delivered to the separation medium (6) is assigned to the separating structure (1),

d) the separating structure (1) is designed in such a way that at least one or more of the following physical or chemical parameters can act on the samples: an electric field, a pressure gradient, an osmotic force, gravity, centrifugal force, and

e) a device for detecting the sample fractions or a device for preparatively collecting said sample fractions is assigned to the separating structure (1).

42. The device as claimed in claim 41, characterized in that an online detection apparatus which records emitted radiation only of an essentially planar detection area (8), preferably close to an interface layer of the separation medium (6) through which interface layer the sample fractions migrate, is assigned to the separating structure (1).

43. The device as claimed in claim 41 or 42, characterized in that a three-dimensional photodetection apparatus capable of detecting the sample fractions in the entire separation body or in a partial volume thereof in the manner that one intensity and one three-dimensional position vector is assigned to each volume element of the separation body is assigned to the separating structure (1).

44. The device as claimed in one or more of claims 41 to 43, characterized in that a fraction-collecting device which comprises:

a) a transport mechanism for plates or layers, for example membranes, which are periodically changed by said transport mechanism at an interface of the separation body so that the sample fractions eluting there are bound on different plates or subareas of a layer or membrane, depending on the retention time, or
b) a capillary array with inlets close to an interface of the separation medium (6) and outlets via a fraction-collecting device, preferably a fraction-collecting device for microtiter plates, so that the sample fractions when eluting from the separation body can be directed through the capillary array out of the separating structure (1), preferably by connecting a pneumatic system or by electric fields,

is assigned to the separating structure (1).

45. The device as claimed in one or more of claims 41 to 44, characterized in that the separating structure (1) is designed in such a way that

a) electrodes (4, 5) are located on two sides (end sides) of the hollow space (2),

b) the spaces between electrodes (4, 5) and separation medium (6) can be filled with a liquid, preferably with a buffer medium (31),

c) heat discharge at the end faces is ensured by a temperature-control device containing buffer medium (31) as a heat transport medium which is moved radially (9, 16) from the center (67) to the periphery or in the opposite direction.

46. The device as claimed in claim 45, characterized in that the hollow space (2) is thermally insulated in the radial direction.

47. The device as claimed in claim 45 or 46, characterized in that a profile temperature-control device is provided along the vertical axis (15).

48. The device as claimed in one or more of claims 45 to 47, characterized in that a circulating apparatus, for example a pump, is provided for circulating the buffer medium (31).

49. The device as claimed in one or more of claims 45 to 48, characterized in that the radius-to-length ratio (9, 15) r/Z of the first space (2) is greater than 0.5, preferably greater than 1.

50. The device as claimed in one or more of claims 41 to 44, characterized in that it is possible to build up a gas or liquid pressure, preferably at one of the end faces of the separation medium (6).

51. The device as claimed in one or more of claims 41 to 44, characterized in that the separating structure (1) is designed so as to be capable of being exposed to centrifugal accelerations.

52. The device as claimed in one or more of claims 41 to 51, characterized in that a measuring head, preferably a multiple measuring head (46), in which the object-side focal points of illumination and detection beam paths are (spot-) confocally superimposed is assigned to the separating structure (1).

53. The device as claimed in one or more of claims 41 to 51, characterized in that a measuring head, preferably a multiple measuring head, in which the object-side focal lines of illumination and detection beam paths are (cylindrical-) confocally superimposed is assigned to the separating structure.

54. The device as claimed in one or both of claims 52 and 53, characterized in that the detection apparatus (45) is integrated into one of the electrodes (4, 5) and, together with the latter, carries out a one- or multidimensional scanning movement with respect to the separation medium (6).

55. The device as claimed in one or more of claims 41 to 51, characterized in that a photodetection apparatus (45) is provided which

a) has an illumination apparatus which illuminates an essentially two-dimensional, planar detection area (8) in the separation medium (6) or close to an interface of said separation medium (6), preferably by means of a coherent light source (26) such as, for example, a laser which, for this purpose, is fanned open by appropriate optics or by a scanning movement of a reflector, and

b) has an optical system which projects the detection area (8) in the form of an image (two-dimensionally) onto an image detector (23, 24).

56. The device as claimed in claim 55, characterized in that the optical axis (43) of the detection apparatus (45) is essentially in the same or in the opposite direction of the direction of sample migration (14), and the optical axis (43) of the illumination apparatus is essentially perpendicular to the direction of sample migration (14).

57. The device as claimed in claim 55, characterized in that the optical axis (43) of the detection apparatus (45) is tilted with respect to the direction of sample migration (14), and the optical axis of the illumination apparatus (26) is essentially perpendicular to the direction of sample migration (14) or that the optical axis of the illumination apparatus (26) is likewise tilted with respect to the direction of sample migration (14), for example perpendicular to the optical axis of the detection apparatus (45).

58. The device as claimed in claim 56 or 57, characterized in that a data recorder (30) which records data during the separation process (in the manner of an online detection) is connected to the detection apparatus (45).

59. The device as claimed in claim 55 for recording a three-dimensional image as

claimed in claim 43, characterized in that

a) the optical axis (43) of the detection apparatus (45) is tilted with respect to the optical axis of the illumination apparatus (26), preferably perpendicular with respect to the optical axis (43) of the illumination apparatus (26),

b) the image-taking device (23) has a translation mechanism which can carry out a relative translational movement, preferably with respect to the separation medium (6),

c) the image-taking device (23) has a data recorder which records data during the translational movement.

60. The device as claimed in one or more of claims 41 to 59, characterized in that a mold section for preparing two-dimensionally arranged depressions in one of the interfaces of the separation medium (6) or in a separate layer (sample plate) is assigned to the separating structure (6).

61. The device as claimed in claim 60, characterized in that the separate layer (sample plate)

a) extend essentially across two dimensions, and
b) are, preferably completely or partially, composed of porous or permeable material and may contain pores,
c) are designed in such a way that samples can be fixed locally therein,
d) are designed so as to enable sample transport in the direction of the surface normal or in the direction opposite to the surface normal or preferably in both directions,
e) are temperature-resistant,
f) are suitable for at least one cell culture,
g) contain a medium suitable for separating sample mixtures, and
h) are transparent.

62. The device as claimed in claim 61, characterized in that depressions are arranged 2-dimensionally on its surface.

63. The device as claimed in one of claims 61 and 62, characterized in that electrodes

or magnetic or magnetizable particles are two-dimensionally arranged in it or on its surface.

64. The device as claimed in one or more of claims 61 to 63, characterized in that the sample plates contain a medium suitable for separating sample mixtures, for example agarose or polyacrylamide.

65. The device as claimed in one or more of claims 61 to 64, characterized in that they are assigned to a device as claimed in one or more of claims 41 to 52.

66. The device as claimed in one or more of claims 61 to 65, characterized in that they are used in a process as claimed in one or more of claims 1 to 40.

67. A device for filling sample plates to be used in a process as claimed in one or more of claims 1 to 40, characterized in that

a) the particles controlled by a sorter, for example an FACS device, or a cell sorter are selected, for example by deflecting in the direction of a pinhole diaphragm, and

b) the selected particles are positioned on the sample plate by means of a translation device whose translational movement is controlled by the sorter.

68. The device as claimed in one or more of claims 41 to 67, characterized in that a regular arrangement (array) of hollow bodies, tips or capillaries suitable for delivering or removing samples is assigned to the separating structure (1) or the sample plates, characterized in that volumes can be shifted, for example by means of a connection to a pneumatic system, or that electric field forces can act by way of mediation through an electrical contact.

69. The use of the process as claimed in one or more of the preceding claims 1-40, characterized in that it is used for fractionating and analyzing biological material.